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Ring-Constrained (N)-Methanocarba nucleosides as adenosine receptor agonists: independent 5'-Uronamide and 2'-deoxy modifications

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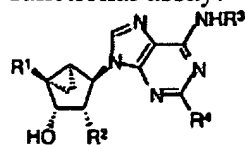
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Abstract

Novel methanocarba adenosine analogues, having the pseudo-ribose northern (N) conformation preferred at adenosine receptors (ARs), were synthesized and tested in binding assays. The 5'-uronamide modification preserved [*N*⁶-(3-iodobenzyl)] or enhanced (*N*⁶-methyl) affinity at A₃ARs, while the 2'-deoxy modification reduced affinity and efficacy in a functional assay.

Graphical Abstract

Novel methanocarba adenosine analogues, having the pseudo-ribose northern (N) conformation preferred at adenosine receptors (ARs), were synthesized and testing in binding assays. The 5'-uronamide modification preserved [*N*⁶-(3-iodobenzyl)] or enhanced (*N*⁶-methyl) affinity at A₃ARs, while the 2'-deoxy modification reduced affinity and efficacy in a functional assay.



R¹ = CH₂OH, CONH-alkyl
 R² = OH, H
 R³ = H, CH₃, cyclopentyl, 3-I-benzyl
 R⁴ = H, Cl



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